

Date of Deposit: October 30, 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Thaddeus P. Dryja et al.

Art Unit: 1631

Serial No.: 09/387,158

Examiner: M. Zeman

Filed : August 31, 1999

Title: RETINOBLASTOMA NUCLEIC ACIDS

Commissioner for Patents
Washington, D.C. 20231**DECLARATION OF THADDEUS P. DRYJA, M.D.**

I declare:

1. I am an inventor of the subject matter claimed in the above-captioned patent application.
2. A written description of 'an isolated nucleic acid molecule that is complementary to a 4.7 kb retinal mRNA present in a cellular sample isolated from a human lacking symptoms of retinoblastoma (Rb) neoplastic disease is provided by the restriction map shown in Fig. 1 of the above-captioned application, as well as in Fig. 2 of parent application Serial No. 06/895,163, filed August 11, 1986). The genetic locus for the Rb gene could be distinguished from any non-Rb genetic locus by the structural characterizations of this restriction map.

3. In 1986, one of ordinary skill in the art would regard a map of restriction enzyme cleavage sites ('restriction map') as a reliable method of structurally identifying and defining a gene. Although nucleotide sequencing was routine in 1986, it was somewhat slow. A restriction map was regarded as the state of the art method for structurally describing a gene.

In fact, the highest standards for structurally describing genes were exemplified by the editors of the well-regarded and peer-reviewed journal *Nature*. In 1986, *Nature* routinely accepted papers for publication which used restriction maps to describe the structure of a gene. *Nature's* standard was met when we published our isolation of the Rb gene in *Nature's* October 16, 1986 issue. Exhibit 1 (Friend et al., *Nature*, 323:643, 1986). *Nature's* standard was

13
Plunked
12/23/01

also met by the Kunkel group when they published the isolation of the Duchenne muscular dystrophy cDNA; the Kunkel group used a restriction map to structurally describe the Duchenne muscular dystrophy cDNA. Exhibit 2 (Monaco et al., *Nature*, 323:646, 1986). *Nature's* standard that restriction maps structurally describe a gene illustrates the standard used, and the level of skill in the art, in 1986.

4. In my considerable experience with restriction mapping I have never known two different genes to have the same restriction map. In fact, a restriction map is routinely used by those skilled in the art to distinguish one cloned gene from another cloned gene.

5. Prior to filing our parent application, we were in possession of several Rb cDNA clones which all shared the same restriction maps, and had confirmed the identity of these clones to be Rb cDNA. This fact was described in our parent specification at page 5, lines 12-13.

6. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Dr. Thaddeus P. Dryja, M.D.

Date: _____